REMARKS

Claims 39-45 were pending in this application. Applicants have amended Claims 39-40 with the recitation "wherein said polypeptide inhibits VEGF stimulated proliferation of endothelial cell growth," support for which is found in the instant specification in Example 66, entitled: "Ability of PRO Polypeptides to Inhibit Vascular Endothelial Growth Factor (VEGF) Stimulated Proliferation of Endothelial Cell Growth (Assay 9)." This assay is also disclosed in International application PCT/US98/19330 filed 9/16/1998, (see Example 66 of the PCT/US98/19330 Specification, pages: 170- 172, Copy enclosed).

The Examiner had already acknowledged enablement for PRO217 (also claimed in the instant application) based on assay #9, in Application 09/904,485, filed July 13, 2001 (now abandoned); for instance, see Office Actions dated October 2, 2002, July 15, 2003 of 09/904,485 application. Applicants believe that the present amendments to claims (based on assay #9) should render claims in better condition for allowance.

The foregoing amendments to the specification are fully supported by the specification and claims as filed and do not constitute new matter. Applicants expressly reserve the right to pursue any canceled matter in subsequent continuation, divisional or continuation-in-part applications.

I. Specification

i) The title of the present application has been amended to clearly indicate the invention to which the claims are directed.

ii) The Examiner objects to embedded hyperlinks and/or browser executable code in the specification.

Applicants fully complied with this requirement in their Preliminary amendment filed March 9, 2004, but that amendment was not entered. The specification has once again been amended to delete references to embedded hyperlinks and/or browser-executable code. Further, the paragraph starting on page 251, line 10 of the specification has been amended to comply with the provisions of the Budapest Treaty.

(iii) The disclosure was objected to allegedly because "several pages have large blank portions (see page 95 and 90). Additionally, pages 78-98 are directed to Tables that have formatting problems (lines wrap to include characters on empty lines)" (Page 4 of the instant specification).

Applicants have carefully reviewed the specification and respectfully submit that no information is missing from the specification as originally filed, although the application has the above-mentioned blank portions and pagination errors in Tables. The blank portions were included in the filed specification simply due to printing errors. Accordingly, the correction of the specification is not necessary. However, if the Examiner still considers that a substitute specification is necessary, Applicants will file the substitute specification upon the Examiner's request.

II. Priority

The Examiner states that Applicants are only entitled to the priority of PCT application PCT/US00/04414 filed February 22, 2000.

Applicants have amended claims to rely on utility based on Assay #9 "Inhibition of VEGF stimulated proliferation of endothelial cells," (instead of previous assay "c-fos inhibition"), and since reference to assay #9 is found in PCT/US98/19330 **filed 9/16/1998**, (see pages 170- 173, Example 66, of the PCT/US98/19330 specification, copy enclosed). Applicants have claimed proper priority to PCT/US98/19330 and submit that it has patentable utility/enablement based on assay#9, for the reasons discussed below. Therefore, Applicants should be entitled to a priority date of **9/16/1998** for the instantly claimed subject matter.

III. Inventorship Correction

An amendment to correct inventorship was filed concurrent with the Preliminary Amendment of June 28, 2006 (see transmittal filed on June 28, 2006). However, this inventorship amendment was neither acknowledged by the Examiner, nor is it reflected on PAIR. Therefore, Applicants submit a new inventorship amendment under 37 C.F.R. § 1.48 (b), based on the instant claim amendments. Applicants respectfully request its consideration.

IV. 35 U.S.C. §112- Enablement

The Examiner rejected claims 39-45 based on the "induction of c-fos" utility (Example 84), and cited references like Hess *et al.,* Suzuki *et al.,* Milde-Langosch *et al.*, indicating that the instant specification did not teach that the polypeptide of SEQ ID NO: 4 had "induction of c-fos"

activity, which was not found on page 215 of the instant specification (see Page 3 of the instant Office Action).

Without acknowledging to the propriety of this rejection, Applicants have amended Claims 39-40 with a recitation based on a different utility, which is disclosed in the instant specification in Example 66, entitled: "Ability of PRO Polypeptides to Inhibit Vascular Endothelial Growth Factor (VEGF) Stimulated Proliferation of Endothelial Cell Growth (Assay 9)." The amended claims now recite "wherein said polypeptide **inhibits VEGF stimulated proliferation of endothelial cell growth**." Hence, any rejection directed to the "induction of c-fos" utility is moot, and Applicants have not argued references Hess *et al.*, Suzuki *et al.* or Milde-Langosch *et al.* herein, since they collectively address the c-fos assay.

Accordingly, based on the "Ability of PRO Polypeptides to Inhibit Vascular Endothelial Growth Factor (VEGF) Stimulated Proliferation of Endothelial Cell Growth (Assay 9)" utility, the rejections to claims 39-45 under 35 U.S.C. §112, first paragraph are overcome.

V. Claim Rejections under 35 U.S.C. §112- Written Description

Claims 39-45 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the Examiner asserts that "(t)he only PRO polypeptide which tested positive in this ("c-fos") assay is PRO287" (Page 5 of the instant Office Action).

As discussed above, Applicants have amended Claims 39-40 with the recitation "wherein said polypeptide **inhibits VEGF stimulated proliferation of endothelial cell growth**," support for which is found in the instant specification in Example 66.

The instantly pending claims recite polypeptides having 95% or 99% sequence identity with the disclosed polypeptide sequence SEQ ID NO: 4, that also recites the functional recitation: "wherein said polypeptide **inhibits VEGF stimulated proliferation of endothelial cell growth**." Example 66 of the present application provides detailed protocols for the VEGF stimulation of endothelial cell growth assay, including the extensive step-by-step guidance in the specification. Applicants claim only those proteins which meet both recitations of the claims, structural and functional. The specification further describes methods for the determination of percent identity between two amino acid sequences (See page 67, line 34, to page 69, line 24). In fact, the specification teaches specific parameters to be associated with the term "percent

identity" as applied to the present invention. The specification further provides detailed guidance as to changes that may be made to a PRO polypeptide without adversely affecting its activity (page 112, line 37 to page 115, line 8). This guidance includes a listing of exemplary and preferred substitutions for each of the twenty naturally occurring amino acids (Table 6, page 114). Accordingly, one of skill in the art could identify whether a variant PRO217 sequence falls within the parameters of the claimed invention. Once such an amino acid sequence is identified, the specification sets forth methods for making the amino acid sequences (see page 112, line 37 to page 116, line 35) and methods of preparing the PRO polypeptides (see page 116, line 37 and onward).

Based on the detailed description of the cloning and expression of variants of PRO217 in the specification, the description of the VEGF stimulation of endothelial cell growth assay, the description of testing for variant polypeptides in the assay, the actual reduction to practice of sequence SEQ ID NO: 4 and the functional recitation in the instant claims, Applicants submit that the specification provides ample guidance such that one of skilled in the art would know that Applicants possessed the invention as claimed in the instant claims, at the time of filing of the application.

For at least the above reasons, withdrawal of the written description rejection of Claims 39-40 under 35 U.S.C. §112, first paragraph, is respectfully requested.

VI. Claim Rejections under 35 U.S.C. §102

(i) Claims 39-40, 42 and 44-45 were rejected under 35 U.S.C. §102(a) as allegedly being anticipated by Hsieh *et al.* (Nature 398: 431-36, 1999) which discloses a polypeptide with 99.7% sequence identity to SEQ ID NO: 4 of the present application. (Page 6 of the instant Office Action).

In view of the discussions above under priority, the "Inhibition of VEGF stimulated proliferation of endothelial cells assay" provides patentable utility for the instant application, and is entitled to a priority date of **September 16, 1998**. The reference date of Hsieh is 1999 which is after the effective filing date of the present application. Thus, Applicants submit that Hsieh is not prior art under §102(a).

Hence, Applicants respectfully request withdrawal of this rejection.

(ii) Claims 39-45 were rejected under 35 U.S.C. §102(a) as allegedly being "anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Hsieh *et al.* (Nature 398: 431-36, 1999)." (Page 6 of the instant Office Action).

Again, for the reasons discussed above, Hsieh is not prior art under §102(a) nor under §103(a), and hence, Applicants respectfully request withdrawal of this rejection.

(iii) Claims 39-40, 42 and 44-45 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Brewer *et al.* (WO 98/54963; published December 10, 1998) which discloses a polypeptide approximately 99% identical to polypeptide of SEQ ID NO: 4 of the present application. (Page 7 of the instant Office Action).

Again, as discussed above, the effective filing date of the present application is **September 16, 1998**. The effective reference date of Brewer is December 10, 1998 which is after the effective filing date of the present application.

Thus, Applicants submit that Brewer is not prior art under 35 U.S.C. §102(b) and respectfully request withdrawal of this rejection.

(iv) Claims 39-45 were rejected under 35 U.S.C. §102(b) as allegedly being "anticipated by or, in the alternative, under 35 U.S.C. §103(a) as obvious over Brewer *et al.* (WO 98/54963; published December 10, 1998)." (Page 8 of the instant Office Action).

Again, Brewer is not prior art under 35 U.S.C. §102(b) nor under §103(a), hence Applicants respectfully request withdrawal of this rejection.

CONCLUSION

The present application is believed to be in prima facie condition for allowance, and an early action to that effect is respectfully solicited. Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney's Docket No. 39780-1618 P2C1-1).

Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: July 5, 2007

J. P. Bernhardt

Jeff Bernhardt (Reg. No. 54,997)
on behalf of Daphne Reddy (Reg. No. 53,507)

HELLER EHRMAN LLP
Customer No. 35489
275 Middlefield Road
Menlo Park, California 94025
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

SV 2287291 v1
7/5/07 9:50 AM (39780.1618)